UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/024,997	12/18/2001	Judy Ruckman	NEX82/D	8763

25871 7590 09/07/2004

SWANSON & BRATSCHUN L.L.C.
1745 SHEA CENTER DRIVE
SUITE 330
HIGHLANDS RANCH, CO 80129

EXAMINER	
FORMAN, BETTY J	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 09/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/024,997	RUCKMAN ET AL.	
	Examiner	Art Unit	
	BJ Forman	1634	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4 and 5* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4 and 5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

FINAL ACTION

Status of the Claims

1. This action is in response to papers filed 29 June 2004 claim 3 was canceled and the previous rejections were traversed.

The previous rejections in the Office Action dated 29 December 2003 under 35 U.S.C. 112, first paragraph are maintained. Applicant's arguments have been thoroughly reviewed and are discussed below.

Claims 4-5 are under prosecution.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 4-5 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 4 is drawn to a method for detecting a deep vein thrombosis in an individual comprising providing a nucleic acid ligand to a β_3 integrin.

Claim 5 is drawn to an anti-clotting composition for use in acute coronary syndromes and percutaneous coronary intervention comprising a nucleic acid ligand to β_3 integrin.

While the specification is enabling for the detecting a nucleic acid ligand for β_3 integrin, the specification does not enable one skilled in the art to which it pertains or with which it is most nearly connected to make or use the invention commensurate in scope with the claims. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirements and whether undue experimentation would be required to make and use the claimed invention (see *In re Wands*, 858 F. 2d 731, 737, 8 USPQ 2d 1400, 1404, 1988). These factors include but are not limited to:

Breadth of the Claims

The claims are drawn compositions comprising and methods of using a nucleic acid ligand to β_3 integrin.

The claims are written so broadly so as to encompass any and all nucleic acid ligands to β_3 integrin. The specification teaches Tables 1-3 comprising 114 nucleic acid ligands to β_3 integrin. The specification suggests that identified ligands have use as therapeutic and diagnostic agents (page 21, second paragraph). The specification merely teaches use of a single nucleic acid ligand for to β_3 integrin (i.e. Aptamer 17.16). And the specification merely teaches in vitro binding of Aptamer 17.16 to human platelets (Example 5) and localization of Aptamer 17.16 to an induced blood clot in a rabbit (Example 6).

The claims are broadly drawn to ANY nucleic acid ligand to β_3 integrin for treating deep vein thrombosis, detecting deep vein thrombosis and as an anti-clotting agent. While the specification, as most, teaches 114 nucleic acid ligands and illustrates localization of Aptamer 17.16 to human platelets and induced blood clots in rabbits, the specification has not taught

this localization of the broadly claimed ligands nor has the specification taught the enormous number of claimed ligands.

Therefore, the specification does not enable one of skill in the art to make and use the broadly claimed invention.

Nature of the Invention

The claims are drawn compositions comprising and methods of using a nucleic acid ligand to β_3 integrin for treating deep vein thrombosis, detecting deep vein thrombosis and as an anti-clotting agent.

The nature of the invention is such that treatment and detection of a medical condition would require a teaching of a relationship between the claimed nucleic acid ligand to β_3 integrin and the medical condition.

The specification teaches Tables 1-3 comprising 114 nucleic acid ligands to β_3 integrin. The specification suggests that the identified ligands have use as therapeutic and diagnostic agents (page 21, second paragraph). The specification merely teaches use of a single nucleic acid ligand for to β_3 integrin (i.e. Aptamer 17.16). And the specification merely teaches in vitro binding of Aptamer 17.16 to human platelets (Example 5) and localization of Aptamer 17.16 to an induced blood clot in a rabbit (Example 6). The specification provides **no** teaching of treating deep vein thrombosis, **no** teaching of detecting deep vein thrombosis in an individual and **no** teaching of anti-clotting applications.

The specification does not teach a relationship between claimed nucleic acid ligands to β_3 integrin and treating deep vein thrombosis, detecting deep vein thrombosis and as an anti-clotting agent.

Therefore, in view of the nature of the invention, the specification does not enable one of skill in the art to make and use the invention as claimed.

Level of Predictability in the Art

The claims are drawn compositions comprising and methods of using a nucleic acid ligand to β_3 integrin for treating deep vein thrombosis, detecting deep vein thrombosis and as an anti-clotting agent.

The level of predictability in the art is very low because the relationship between the claimed nucleic acid ligands to β_3 integrin and treatments is undefined as evidenced by the specification's suggestion that the identified ligands have use as therapeutic and diagnostic agents (page 21, second paragraph). Because the claims are drawn to any nucleic acid ligand to β_3 integrin and because methods of treating deep vein thrombosis, detecting deep vein thrombosis and as an anti-clotting agent would require a nexus between the claimed ligands and the claimed methods and composition goals, the predictability that any nucleic acid ligand to β_3 integrin would accomplish those methods and/or goals is very low.

Therefore, the level of predictability for the instantly claimed invention is very low.

Existence of Working Examples

The claims are drawn compositions comprising and methods of using a nucleic acid ligand to β_3 integrin for treating deep vein thrombosis, detecting deep vein thrombosis and as an anti-clotting agent.

The specification teaches Tables 1-3 comprising 114 nucleic acid ligands to β_3 integrin. The specification suggests that the identified ligands have use as therapeutic and diagnostic agents (page 21, second paragraph). The specification merely teaches use of a single nucleic acid ligand for to β_3 integrin (i.e. Aptamer 17.16). And the specification merely teaches *in vitro* binding of Aptamer 17.16 to human platelets in culture (Example 5) and localization of Aptamer 17.16 to an induced blood clot in a rabbit (Example 6).

The specification provides no working examples of treating deep vein thrombosis with a composition comprising nucleic acid ligands to β_3 integrin, no working examples of detecting deep vein thrombosis in an individual using nucleic acid ligands to β_3 integrin and no working examples of an anti-clotting composition comprising nucleic acid ligands to β_3 integrin. Furthermore, the specification provides no working examples of treating deep vein thrombosis, no working examples of detecting deep vein thrombosis in an individual and no working examples of an anti-clotting composition useful in acute coronary syndromes or percutaneous coronary intervention.

Therefore, the specification does not provide working examples of the claimed invention which would enable one of ordinary skill in the art to make and use the invention as claimed.

Quantity of Experimentation Required

The claims are drawn compositions comprising and methods of using a nucleic acid ligand to β_3 integrin for treating deep vein thrombosis, detecting deep vein thrombosis and as an anti-clotting agent.

In view of the breadth of the claims being drawn any nucleic acid ligand to β_3 integrin; in view of the nature of the invention in which treatment and detection of a medical condition would require a teaching of a relationship between the claimed nucleic acid ligand to β_3 integrin and the medical condition and the lack of such a teaching in the specification; in view of the of unpredictability in the art with regard to treatment and detection of a medical condition without a known relationship between the ligand and the condition; and in view of the lack of working examples of the broadly claimed invention, it would require undue experimentation for one skilled in the art to make and use the invention as claimed.

Response to Arguments

4. Applicant asserts that the specification and prior art provide evidence of a correlation between β3 integrin binding and DVT detection in individuals as exemplified by radiolabeled fibrinogen and thrombin which bind α_{IIb} β3. The argument has been considered but is not found persuasive. While a correlation between α_{IIb} β3 binding and DVT detection is exemplified in the art, the claims are drawn to "nucleic acid ligands to a β3 integrin". As stated above, specification merely teaches use of a single nucleic acid ligand binding β_3 integrin (i.e. Aptamer 17.16). The claimed method requires in vivo administration and detection of a nucleic acid ligand to a β3 integrin. While the specification teaches in vivo administration and detection of Aptamer 17.16 in rabbits and further teaches selection of additional nucleic acid ligands that bind β_3 integrin in Tables 1-3, the specification does not teach which of the nucleic acid ligands bind in vitro as required by the instant methods.

Applicant asserts that the in vivo example provided in the specification suffices to enable the instantly claimed method for human application. The argument has been considered but is not found persuasive because, as stated above, the specification has exemplified a single ligand that binds rabbits in vivo. The genus of claimed ligands bind β3 integrin in an individual. The specification does not provide a comparison between human and rabbit β3 integrin such that one of skill in the art would expect all ligands to rabbit β3 integrin to bind equally to human β3 integrin whereby the rabbit example in the specification would exemplify a human model. Furthermore, the specification does not provide guidance on selecting other ligands that bind in vivo, the conditions required to do so, or criteria that the selected ligands must meet to be useful as claimed.

Applicant states that the specification teaches that α_{IIb} β3 is a major integrin on the surface of platlets where it mediates adhesion during clot formation and further teaches examples of α_{IIb} β3 binding molecules which are approved anti-clotting drugs. Applicant asserts that these facts support a correlation between β3 binding molecules and anti-clotting

activity. The arguments have been considered but are not found persuasive. While the specification does teach an example of Aptamer 17.16 binding to activated platelets, the specification has not provided a single example of anti-clotting (in vivo **or** in vitro) and the specification has not illustrated that Aptamer 17.16 or any of the claimed ligands share a structure or binding function equal or similar to those of the approved anti-clotting drugs. Hence, the specification does not enable one of skill in the art to make and use the invention as claimed.

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

6. No claim is allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741. The examiner can normally be reached on 6:00 TO 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

BJ Forman, Ph.D.
Primary Examiner
Art Unit: 1634
September 3, 2004